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Research Article

MICROWAVE ASSISTED SOLVENT FREE SYNTHESIS AND EVALUATION OF ANTIMICROBIAL AND ANTIOXIDANT ACTIVITIES OF SOME NOVEL 3, 4-BIS (SUBSTITUTED PHENYL)-7-(6-METHYL PYRIDIN-2-YL)-3, 3A, 3B, 4-TETRAHYDRO-7H-PYRROLO [2, 3-C : 5,4-C']DIISOXAZOLE

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ABSTRACT
Novel heterocyclic compounds were synthesized, characterized and screened for antimicrobial activity and antioxidant activity. This series of novel bis-isoxazole derivatives were synthesized via reaction of bis chalcone of succinimide treated with hydroxyl amine hydrochloride in presence of neutral alumina by microwave assisted solvent free method in good yield. It was observed that microwave assisted method produced a greater yield of products in shorter reaction times. The structures of synthesized compounds were characterized by their spectral analyses (elemental analysis, FTIR, ^{1}H NMR) and the purity of synthesized compounds were confirmed by TLC. All the synthesized compounds were evaluated for antimicrobial activity against gram positive bacteria *Staphylococcus aureus* (NCIM 2079) and gram negative bacteria *Escherichia coli* (NCIM 2109) using DMSO solvent and antifungal activity against fungal strain *Aspergillus Niger* (NCIM 545). Most of the synthesized compounds exhibited a moderate grade of anti-microbial activity. The study concluded that the compound 4c exhibited potent anti-bacterial activity when compared to Chloramphenicol as standard drug while compound 4b, 4c, 5b, 5c, 5e exhibited significant anti-fungal activity when compared to Amphotericin B as standard drug. All the synthesized compounds were screened for their antioxidant activities. Among them, compounds 4a, 4e, 5a, 5b, 5c and 5e showed moderate to good antioxidant activity when compared to ascorbic acid as standard drug.

Keywords: Succinic anhydride, 1-(6-Methylpyridin-2-yl) Pyrrolidine-2, 5-Dione, Bis-chalcone, Bis-isoxazole, Antimicrobial activity, Antioxidant activity.

1. INTRODUCTION
Cyclic imides, for instance, succinimides and glutarimides are vital category of heterocyclic compounds through several pharmacological applications in different fields. The chalcones are aromatic α, β-unsaturated ketones containing the reactive-COCH=CH- moiety, the presence of α, β-Unsaturated carbonyl system in chalcones makes variety of important biologically active compounds. Chalcones are used as intermediary for the synthesis of compounds having therapeutic significance. Chalcones are the precursor of flavonids and isoflavonoids that are usually present in edible plants.
An isoxazole (C_3H_3NO) is a five member heterocycle molecule containing oxygen and nitrogen atom at 1 and 2 positions. This compound is used for synthesis of antibiotic, antitumor, anti-HIV, anti fungal agents. Many classes of chemotherapeutic agents contains isoxazole moiety are in chemical uses such as antibacterial agents, anti cancer, antiviral, anti fungal agents, anti malarial agents.
Isoxazole is a promising structural species for drug designing. Isoxazole based heterocycles are potential bioactive molecules and exhibit anti tubercular [1], analgesic [2], antipyretic [2], anti-inflammatory [2,3], anti platelet [4], anti-HIV [4], antagonist activity [4], CNS depressant [5], anti-fungal [6,7], antibacterial [6-8,14-

20], anti-oxidant [7], anti-cancer [9,10] activity. Encouraged by the wide range of biological activities of isoxazole heterocyclic compounds, it was determined to synthesize a new series of isoxazole derivatives. Literature survey revealed that isoxazole heterocyclic moiety represents a core structure for number of drugs. Recently, isoxazole derivatives seek huge attention of researchers in organic and medicinal chemistry due to their prompt biological and pharmacological importance. Encouraged by the therapeutic variety of isoxazole containing moiety, we took up the synthesis of certain novel isoxazole derivatives and evaluated for their antimicrobial, antifungal and antioxidant activities.

2. MATERIAL AND METHODS

The melting point of synthesized compounds was determined by open capillary tubes and was uncorrected (Melting point expressed in degree Celsius). TLC was used to check and confirm the purity of all synthesized compounds and to monitor the reactions as well using suitable solvents. The IR spectra were taken on FTIR Agilent technologies spectrometer at 4000-650. The ^{1}H NMR were recorded on 500 MHz by Bruker spectro-photometer .The chemical shifts are expressed in ð ppm, using tetra methyl silane (TMS) as internal reference.

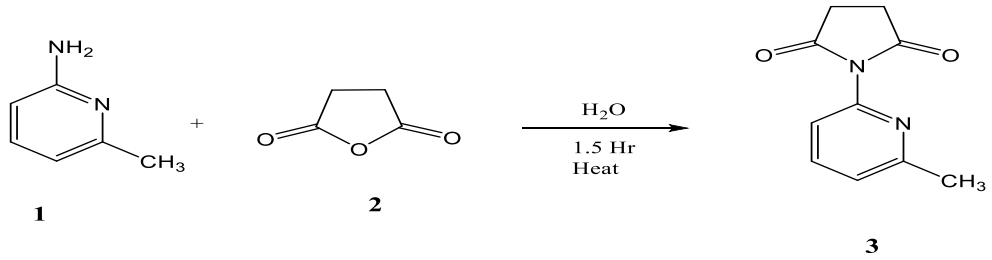
2.1. General Procedure of Synthesis

2.1.1. Preparation of 1-(6-Methylpyridin-2-yl) pyrrolidine-2, 5-dione (3)

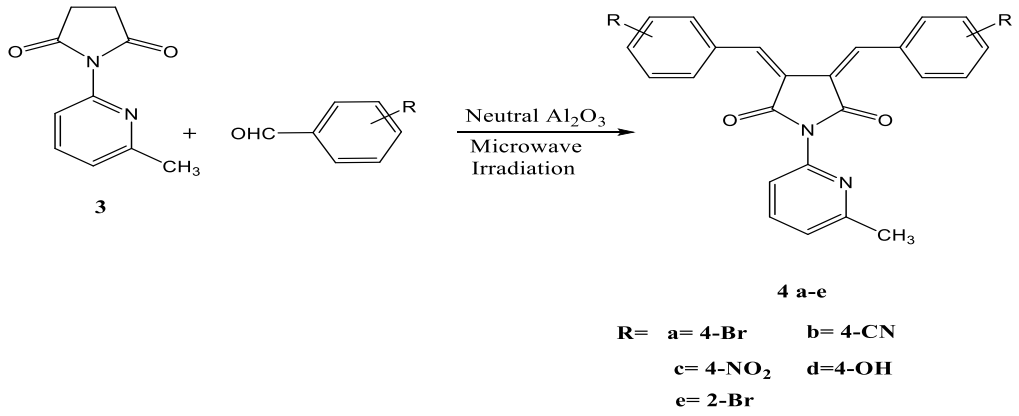
A 0.01 mole of 6-methyl 2-amino pyridine was dissolved in 20 ml of water and 0.01 mole of succinic anhydride was slowly added. The mixture was heated in oil bath with concurrent distillation of water. The water was totally removed, the temperature of the reaction mixture was maintained at 180°C for about 1.5 hr. The crude product was separated and recrystallized from isopropyl alcohol (Scheme-1).

2.1.2. Preparation of (3Z, 4Z)-1-(6-methyl pyridin-2-yl)-3, 4-bis (Substituted benzylidene) pyrrolidine -2, 5-dione (4 a-e)

The bis-chalcones (4a-e) derivatives were synthesized by the mixture of 0.01 moles N-6-methyl pyridine succinimide and 0.02 mole of substituted benzaldehyde in 1 gm of neutral Al_2O_3 with the assistance of microwave irradiations. The mixture was placed in microwave at 750-850 W power for 3-6 min. in solvent free conditions. The bis-chalcone derivatives were separated. The crude product was washed with hot water for elimination of neutral Al_2O_3 (Scheme-2).



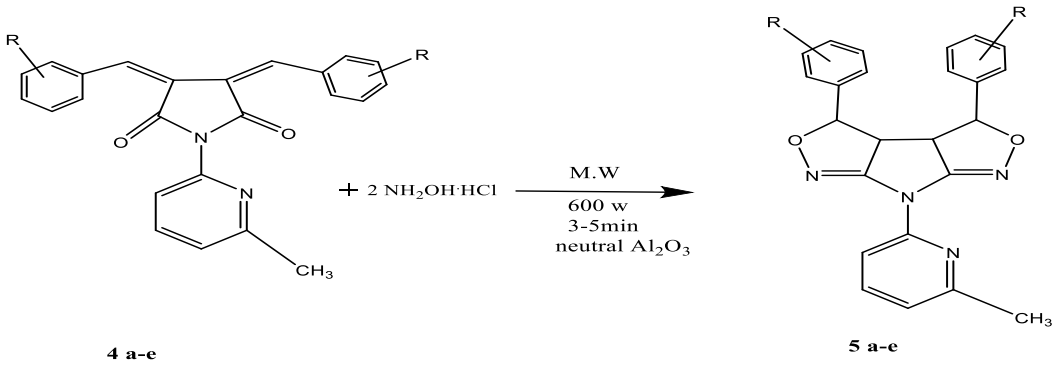
Scheme 1: Preparation of 1-(6-Methylpyridin-2-yl) pyrrolidine-2, 5-dione



Scheme 2: Preparation of (3Z, 4Z)-1-(6-methyl pyridin-2-yl)-3, 4-bis (Substituted benzylidene) pyrrolidine -2, 5-dione

2.1.3. Preparation of 3, 4-bis(substituted phenyl)-7-(6-methyl pyridin-2-yl)-3,3a,3b,4-tetra hydro -7H-pyrrolo[2,3-c:5,4-c'] diisoxazole (5a-e)

The bis-isoxazole derivatives were synthesized by 0.1 mole of bis-chalcone and 0.2 moles hydroxyl amine hydrochloride in 1 gm of neutral Al_2O_3 under microwave supported solvent free condition using 600 W power for 3-5 min. The afforded coloured compounds were recrystallized by ethanol. The purity of synthesized compounds was confirmed by TLC.



4 a-e **5 a-e**

R=
a=4-Br
b=4-CN
c=4-NO_2
d=4-OH
e=2-Br

Scheme 3: Preparation of 3, 4-bis(substituted phenyl)-7-(6-methyl pyridin-2-yl)-3,3a,3b,4-tetra hydro-7H-pyrrolo[2,3-c:5,4-c'] diisoxazole

Table 1: Physical standard of the synthesized compounds (3, 4a-e, 5a-e)

Compound code	Molecular formula	Molecular weight	% Yield	M.P.(°C)	Colour
3	$C_{10}H_{10}O_2N_2$	190.20	78	147-149	Whitish Solid
4a	$C_{24}H_{16}Br_2N_2O_2$	524	89	144-148	Yellowish solid
4b	$C_{26}H_{16}N_4O_2$	416	90	121-124	Yellowish solid
4c	$C_{24}H_{16}N_4O_6$	456	85	127-131	Brownish solid
4d	$C_{24}H_{18}N_2O_4$	398	60	139-143	Light orange solid
4e	$C_{24}H_{16}Br_2N_2O_2$	524	89	82-86	Yellowish solid
5a	$C_{24}H_{18}Br_2N_4O_2$	554.24	80	148-150	Whitish yellow
5b	$C_{26}H_{18}N_6O_2$	446.47	82	132-134	Whitish yellow
5c	$C_{24}H_{18}N_6O_6$	486.44	78	78-81	Yellow
5d	$C_{24}H_{20}N_4O_4$	428.45	76	214-217	Dark Brown
5e	$C_{24}H_{18}Br_2N_4O_2$	554.24	75	170-172	Dark Brownish

2.2. Antimicrobial activities

In our recent study, antibacterial and antifungal activity was evaluated by standard agar diffusion assay. All the newly synthesized compounds were screened for the antibacterial activity against gram positive bacteria *Staphylococcus aureus* (NCIM 2079) and gram negative bacteria *Escherichia coli* (NCIM 2109) using DMSO solvent and antifungal activity against *Aspergillus Niger* (NCIM 545) strains using DMSO solvent. Chloramphenicol was used as a standard drug for antibacterial activities and Amphotericin B was used as standard drug for antifungal activities. Stock solution 1000 microgram per ml of each compound was prepared in DMSO. Assay was carried out by taking concentration 100 microgram per well. Chloramphenicol and Amphotericin B (10 microgram/disk), moistened with water were used as standard. Growth culture for all bacterial strain nutrient agar medium was used. The composition of nutrient agar culture was Sodium chloride-5.0 gm, Beef extract 10.0gm, Peptone 10.0

gm (pH 7.2). For fungi (*Aspergillus niger*) Potato Dextrose agar was used as a growth medium. The medium consist of Potatoes infusion 200gm, Dextrose, 20; Final pH (at 25°C) 5.6±0.2 [24,25]. The antibacterial evaluation revealed that many of the screened compounds showed good zone of inhibition against tested microbial strains as compared to the standard drugs. The synthesized compounds 4c,5c & 5e were observed to be more potent against selected bacterial strains as compared to the standard drugs. The antifungal activities for compounds 4b,4c,5c,5e were active against fungal strains. The activities are represents graphically in graph 01 and graph 02.

2.3. Antioxidant activity

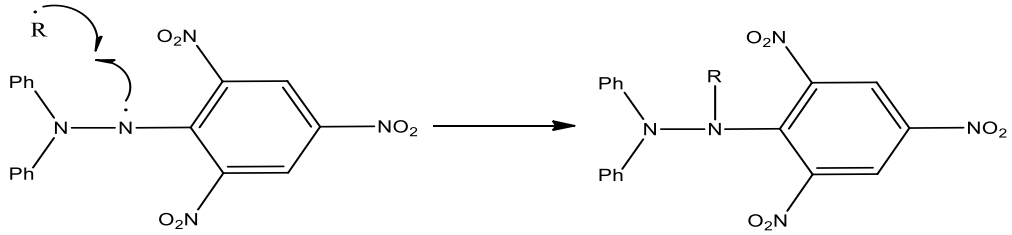
2.3.1. In vitro antioxidant activity of compounds by DPPH assay method

The newly synthesized compounds were evaluated for antioxidant activities by the 2,2-diphenyl-1-picryl-hydrazyl (DPPH) radical scavenging activity. It is a standard test in antioxidant activity studies and offers a fast technique for screening the radical scavenging activity of specific compounds [21].

DPPH radical scavenging activity was done using the reaction mixture containing 1 mL of DPPH solution (2.0 mM /L, in 95% methanol v/v) with 3 mL extract was shaken and incubated for 30 min at room temperature in dark. Subsequent to the incubation, absorbance was examined at 517 nm against blank. Ascorbic acid was taken as a reference standard. The radical scavenging activity was calculated as reduce in the absorbance of DPPH in triplicates and calculated by the following equation:

Scavenging (%)= $\{1-(A_{sample}- A_{control})\}$ x 100

The 2, 2-diphenyl-1-picrylhydrazyl radical (DPPH) has been broadly utilized to evaluate the free radical scavenging capacity of different antioxidants. The resultant changes color from purple to yellow, the reduction in absorbance is observed when the DPPH is scavenged by an antioxidant, during the donation of hydrogen to form a stable DPPH molecule in the radical form. This molecule had an absorbance at 517 nm, which is missing after taking off an electron or hydrogen radical from an antioxidant compound to form the reduced DPPH-R [22, 23].



The compounds **[4a, 5a, 5b, 5e]** shows strong % scavenging activity against standard ascorbic acid at concentrations 200 µg/mL, and **[5a,5b,5e]** shows the potent % scavenging activity at concentrations 400 µg/mL while **[5a,5b]** shows strong % scavenging activity at concentrations 600 µg/mL against standard ascorbic acid due to the presence of cyano and halogens functional group in their structure in graph 03.

2.4. Statistical analysis

The experiments were carried out for the determination of antimicrobial properties of newly synthesized compounds. The experimental statistics were reported as the mean±standard deviation (SD) having six replicates (n = 6). The diameter of zones of inhibition against the elected bacterial strains (*S. aureus* and *E.coli*) and fungal strain (*A.niger*) among samples were screened using Kolmogorov-Smirnov and Shapiro-Wilks at the 95% confidence level. Test of homogeneity of variances among samples was performed using Levene's test. The mean difference amid the groups were examined by Analysis of Variance (ANOVA) followed by Duncan's Post hoc multiple comparison test. 'p' values of $p < 0.01$ and $p > 0.05$ were considered significant.

3. RESULTS AND DISCUSSION

3.1. Chemistry

The cyclic imides were synthesized by reaction of substituted aromatic amine with succinic anhydride. The afforded cyclic imide treated with various substituted aromatic aldehyde furnished a series of bis-chalcones. A series of bis isoxazole were prepared in good yield by cyclization of bis chalcone with hydroxyl amine hydrochloride in presence neutral alumina under solvent

free microwave irradiation. The afforded bis isoxazole were confirmed by IR, ^{1}H NMR and elemental analysis.

3.2. Physiochemical and analytical data for compounds

3.2.1. 1-(6-Methylpyridin-2-yl) pyrrolidine-2, 5-dione(3)

Molecular formula: $C_{10}H_{10}O_2N_2$, Whitish Solid, Percent Yield:78%, Molecular weight: 190.20, Melting point: 147-149°C, Elemental Analysis: Calculated- C 63.13%, H. 5.29%,N. 14.75%,[Found- C. 63.33%, H. 5.08%, N. 14.89%], IR: 1719, 2471, 2928, 1567, 1598, 2749, 1330, 1307, 3030, 2969 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d^6,δ ppm): 2.37(S, 3H, CH_3-Pyridine), 2.89(S, 4H, imide), 7.72-8.38(m, 2H, pyridine), 8.25(d, 1H, pyridine).

3.2.2. (3Z, 4Z)-1-(6-methylpyridin-2-yl)-3,4-bis(4-bromobenzylidene)pyrrolidine-2,5-dione(4a)

Molecular formula: $C_{24}H_{16}Br_2N_2O_2$, Yellowish solid, Percent Yield: 89%, Molecular weight: 524; Melting point: 144-148°C, Elemental Analysis: Calculated-C. 54.93%, H. 3.10%, N. 5.37%, [Found- C. 54.77%, H. 3.38%, N. 5.52%], IR: 1717, 747, 849, 1329, 1309, 3036, 2958, 2929, 1533, 1602, 2717 cm^{-1}. ^{1}H-NMR (500 MHz, DMSO-d^6,δ ppm): 6.47-8.38 (m, 7H, Ar-H and =C-H), 2.61 (S, 3H, -CH_3).

3.2.3. ((3Z, 4Z)-1-(6-methylpyridin-2-yl)-3,4-bis (4-cyanobenzylidene)pyrrolidine-2,5-dione (4b)

Molecular formula: $C_{26}H_{16}N_4O_2$, Yellowish solid, Percent Yield: 90%, Molecular weight: 416, Melting point: 121-124°C Elemental Analysis: Calculated-C. 74.92%, H. 3.81%, N. 13.41%, [Found-C. 74.67%, H. 3.97%, N. 13.59%], IR: 1710, 2477, 2209, 1309, 3039, 2950, 2929, 1549, 1600, 2744 cm^{-1}. ^{1}H-NMR (500 MHz, DMSOd^6,δ ppm): 6.38-8.12 (m, 7H, Ar-H and =C-H), 2.53 (S, 3H, -CH_3).

3.2.4. (3Z, 4Z)-1-(6-methyl pyridin-2-yl)-3,4-bis (4-nitro benzylidene) pyrrolidine-2,5-dione (4c)

Molecular formula: $C_{24}H_{16}N_4O_6$, Brownish solid, Percent Yield:85%, Molecular weight:456, Melting point:127-131°C Elemental Analysis: Calculated-C. 63.19%,H. 3.57%, N. 12.32%,[Found-C. 63.35%, H. 3.29%, N. 12.47%], IR:1719, 1353, 1310, 3051, 2957, 2929, 1598, 2765 cm^{-1}. ^{1}H-NMR (500 MHz, DMSO-d^6,δ ppm): 7.20-8.17 (m,7H, Ar-H and =C-H), 2.50 (S, 3H, -CH_3).

3.2.5. (3Z,4Z)-1-(6-methylpyridin-2-yl)-3,4-bis(4-hydroxybenzylidene)pyrrolidine-2,5-dione (4d)

Molecular formula: $C_{24}H_{18}N_2O_4$, Light orange solid, Percent Yield: 60%, Molecular weight: 398, Melting point: 139-143°C Elemental Analysis: Calculated-C. 72.30%, H. 4.51%, N. 7.09%, [Found-C. 72.47%, H. 4.59%, N. 7.17%], IR: 1700, 1340, 1309, 3111, 2917, 1553, 1600, 2763 cm^{-1}. ^{1}H-NMR (500 MHz, DMSO-d^6,δ ppm): 7.13-8.20 (m, 7H, Ar-H and =C-H), 2.39 (S, 3H, -CH_3), 10.05 (S,1H, OH).

3.2.6. (3Z, 4Z)-1-(6-methyl pyridin-2-yl)-3,4-bis (2-bromo benzylidene) pyrrolidine-2,5-dione (4e)

Molecular formula: $C_{24}H_{16}Br_2N_2O_2$, Yellowish solid, Percent Yield: 89%, Molecular weight: 524, Melting point: 82-86°C, Elemental Analysis: Calculated-C. 54.92%, H. 3.09%, N. 5.39%, [Found-C. 54.60%, H. 3.21%, N. 5.43%], IR: 1719, 740, 861, 2491, 1339, 3049, 2966, 2929, 1555, 1603cm^{-1}. ^{1}H-NMR (500 MHz, DMSO-d^6,δ ppm): 6.97-8.40 (m, 7H, Ar-H and =C-H), 2.53 (S, 3H, -CH_3).

3.2.7. 3,4-bis(4-bromo phenyl)-7-(6-methyl pyridin -2-yl)-3,3a,3b,4-tetrahydro-7H-pyrrolo[2,3-c:5,4-c'] diisoxazole (5a)

Molecular formula: $C_{24}H_{18}Br_2N_4O_2$, Whitish yellow solid, Percent yield: 80 %, Molecular weight: 554.24, Melting point (°C):148-150 °C, Elemental analysis: Calculated-C. 52.01%, H. 3.27%, N. 10.11%, [Found-C. 52.15%, H. 3.39%,N.10.18%], IR:2964, 3055, 1627, 1068, 1309, 716, 1656, 1689 cm^{-1}. ^{1}H NMR (500 MHz,DMSO-d^6,δppm): 2.41 (S,3H,-CH_3), 6.56-8.1(m,7H,Ar-H), 2.40(d,1H, isoxazole).

3.2.8. 4, 4'-(7-(6-methyl pyridin-2-yl)-3,3a,3b,4-tetrahydro-7H-pyrrolo [2,3-c:5,4-c'] diisoxazole-3,4-diyl) dibenzonitrile (5b)

Molecular formula: $C_{26}H_{18}N_6O_2$, Whitish yellow solid, Percent yield: 82 %, Molecular weight: 446.47, Melting point (°C): 132-134°C, Elemental analysis: Calculated-C. 69.95%, H. 4.06%, N. 18.82%, [Found-C. 69.79%, H. 4.27%, N. 18.91%], IR: 2970, 3010, 1652, 1087, 1324, 728, 1650, 1690 cm^{-1}. ^{1}H

NMR (500 MHz, DMSO-d^6, δ ppm): 2.45 (S, 3H,-CH_3), 6.31-7.80(m, 7H, Ar-H), 2.33(d, 1H, isoxazole).

3.2.9. 7-(6-methyl pyridin-2-yl)-3,4-bis(4-nitro-phenyl)-3,3a,3b,4-tetrahydro-7H-pyrrolo [2,3-c:5,4-c']diisoxazole(5c)

Molecular formula: $C_{24}H_{18}N_6O_6$, yellow solid, Percent yield: 78 %, Molecular weight: 486.44, Melting point (°C): 78-81°C, Elemental analysis: Calculated-C. 59.26%, H. 3.73%, N. 17.28%, [Found- C. 59.43%, H. 3.62%, N. 17.41%], IR: 2979, 3017, 1657, 1090, 1329, 732, 1653, 1687cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d^6,δ ppm):2.47 (S,3H,-CH_3),6.29-8.1(m,7H, Ar-H),2.32 (d,1H, isoxazole).

3.2.10. 4, 4'-(7- (6- methyl pyridin-2-yl)-3,3a,3b,4-tetra hydro-7H-pyrrolo[2,3-c:5,4-c']diisoxa-zole-3,4-diyl)diphenol(5d)

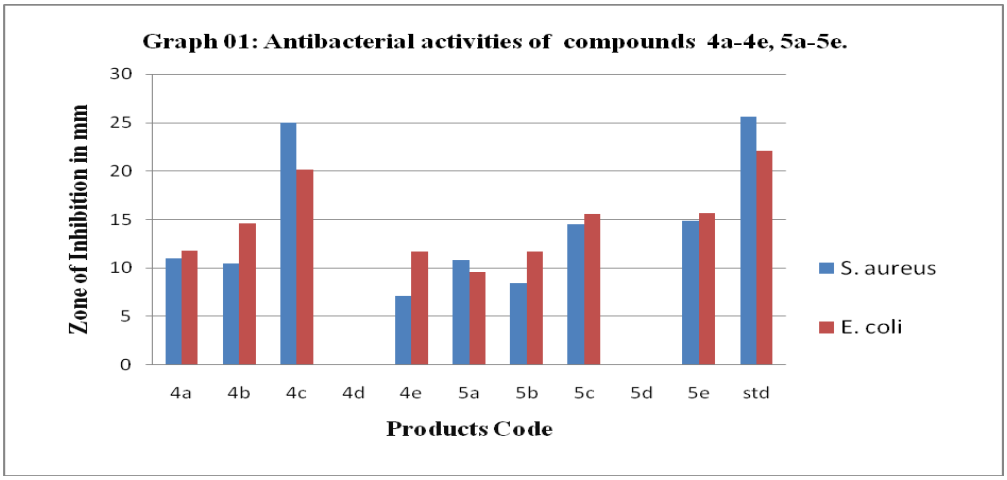
Molecular formula: $C_{24}H_{20}N_4O_4$, Dark Brown solid, Percent yield: 76 %, Molecular weight: 428.45, Melting point (°C):214-217°C, Elemental analysis: Calculated-C. 67.28%, H. 4.71%, N. 13.08%, [Found-C. 67.39%,H. 4.63%,N.13.29%], IR:2958, 3048, 1631, 1064, 1311, 719, 1655, 1691cm^{-1}. ^{1}H NMR (500MHz,DMSO-d^6,δppm): 2.45(S,3H,-CH_3), 6.29-7.10(m,7H,Ar H), 2.34(d,1H,isoxazole), 9.02 (S,1H,-OH).

3.2.11. 3, 4-bis (2-bromo phenyl)-7-(6-methyl-pyridin-2-yl)-3,3a,3b,4-tetra hydro-7H-pyrrolo[2,3-c:5,4-c']diisoxazole(5e)

Molecular formula: $C_{24}H_{18}Br_2N_4O_2$, Dark Brown solid, Percent yield: 75 %, Molecular weight: 554.24, Melting point (°C): 170-172°C, Elemental analysis: Calculated-C. 52.01%, H. 3.27%, N. 10.11%, [Found-C. 52.29%, H. 3.43%,N.10.27%], IR:2930, 3051, 1629, 1071, 1311, 719, 1662, 1688 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d^6, δ ppm): 2.43 (S,3H,-CH_3), 6.31-7.60 (m,7H,Ar-H),2.32(d,1H, isoxazole).

3.3. Antimicrobial activities

The results of antibacterial activity are represented graphically in graph 1. The zone of inhibition was calculated in mm. The activity index of all the synthesized compounds were also intended for bacterial strains against Chloramphenicol as standard. The zone of inhibition ranges generally between 7.1-25.1 for *S.aureus*, 9.61-20.14 for *E.coli*. Majority of the compounds exhibited strong activity against *S. aureus* as compared to standard drug chloramphenicol.



Graph 1: Antibacterial activities of 4a-4e and 5a-5e.

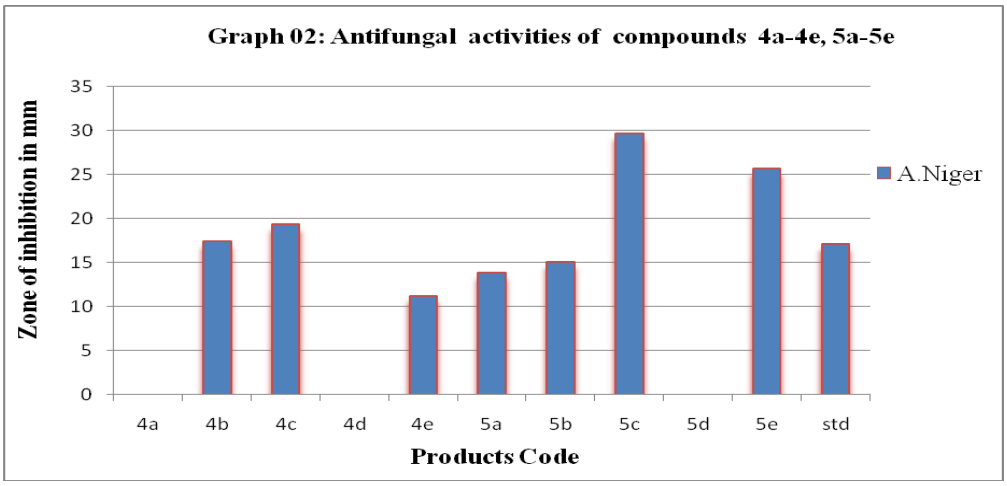
All the tested compounds have exhibited moderate to strong inhibition against *S. aureus* and *E.coli*. Compound **4c** demonstrated promising antibacterial activity against *S. aureus*. Similarly **5c** and **5e** exhibited strong inhibition against *S.aureas*. Similarly compound **4c** demonstrated promising antibacterial activity against *E.coli* and **4b, 5c** and **5e** shown strong inhibition toward *E.coli*. Finally, it can be concluded that all the synthesized compounds tested for antibacterial activity, possess moderate to strong activity as compared to standard chloramphenicol.

The results of antifungal activity of compounds are represented graphically in graph 2 in the form of zone of inhibition. By the observation of the graph, it can be

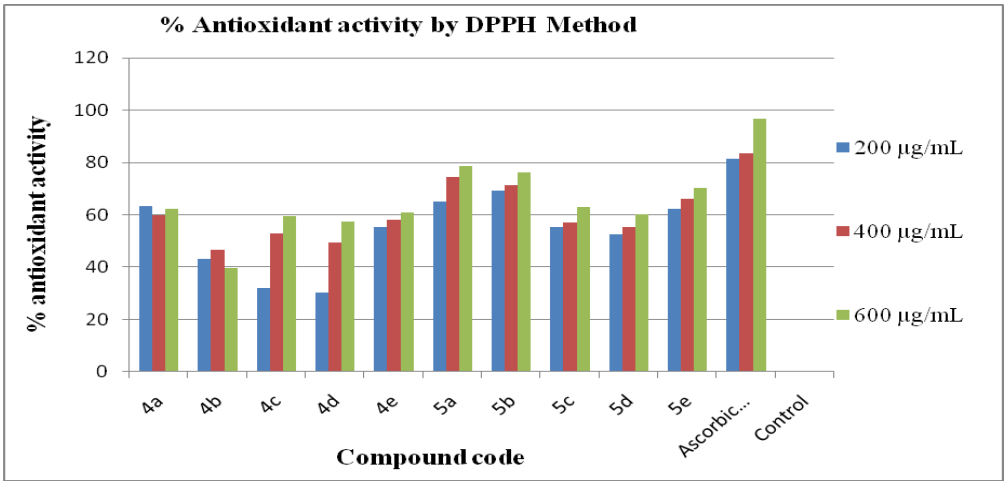
concluded that majority of compounds exhibited moderate to strong activity against *A.niger* fungal strain. Among the tested compounds, highest antifungal activity i.e.29.71 mm and 25.67 mm were exhibited by compounds **5c** and **5e** against *A. niger*. Compound **4b** and **4c** also shown strong zone of inhibition against *A. niger*. Overall antifungal activities of synthesized compounds against *A.niger* fungal strain are moderate to strong as compared to standard Amphotericin B.

3.4. Antioxidant activity

The antioxidant activity was expressed in terms of the concentration (µg/mL) of compound at which DPPH reduction was observed, this may be due to the presence of electron withdrawing substituents such as cyano/halogens at *para* position and the *ortho* position in phenyl ring of bis chalcone and bis isoxazole derivatives as shown in graph 3. The compounds **4a, 5a, 5b, 5e** shown potent antioxidant activity against standard ascorbic acid at concentrations 200 µg/mL, and compounds **5a, 5b & 5e** exhibited the potent % scavenging activity at concentrations 400 µg/mL whereas the compounds **5a, 5b** shows strong % scavenging activity at concentrations 600 µg/mL against standard ascorbic acid in graph 03.



Graph 2: Antifungal activities of 4a-4e and 5a-5e



Graph 3: Antioxidant activities of 4a-4e and 5a-5e.

4. CONCLUSION

The main focus of this research work was the bis-isoxazoles (5a-e) have been synthesized by the treatment of bis-chalcones with hydroxyl amine hydrochloride in presence of neutral alumina by microwave supported solvent free method. The synthesized compounds were characterized by their spectral analysis and screened by antibacterial and antifungal activities as well as antioxidant activity. Microwave method is ecofriendly which can be used for preparation of various

heterocyclic synthons. It was found that the reactions were completed in shorter reaction times, higher yields, in microwave method as compared to conventional methods. From the results, it can be concluded that the modified isoxazoles exhibit significant biological evaluation as anti-microbial agents as well as antioxidant. However, further evaluation of isoxazole will be carried out, concerning the structural arrangements in ring for anti-microbial activity and antioxidant activity.

Conflict of interest

None declared

Source of funding

None declared

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